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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,612	01/26/2006	Gianfranco Gilardi	Q88296	4772

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EXAMINER

MEAH, MOHAMMAD Y

ART UNIT	PAPER NUMBER
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1652

MAIL DATE	DELIVERY MODE
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07/02/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.		Applicant(s)	
	10/537,612		GILARDI, GIANFRANCO	
	Examiner		Art Unit	
	Mohammad Meah		1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 4/17/07
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-5, 12-15 and 21-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 14 is/are allowed.
- 6) ☐ Claim(s) 1-5, 12-13, 15 and 21-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/3/05</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim 1-18 and 20-27 are pending.

With preliminary amendment of this application, the applicant, on date 04/17/2007 elected with traverse Group IV (claims 1-5, 12-13, 14-15 , 21-22 and SEQ ID NO: 11) for examination.

Election/Restriction

Election restriction office action of 01/17/07 erroneously omitted in including claims 23-27 in any groups. Since these claims comprise protein they are grouped as follows: claims 23-25,26 are included in group I, claims 23-25 are included in group II, claims 23-25 and 27 are included in group III and claims 23-25 are included in groups IV.

During preliminary amendment of this application, the applicant, on date 04/17/2007 elected with traverse Group IV (claims 1-5, 12-13, 14-15 , 21-25 and SEQ ID NO: 11) drawn to a protein comprising ROP motif and redox center for examination. Groups 1- III and V-XII (claims 18, 23-27) of election/restriction-office action of date 01/17/07 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Applicants arguments of the claims are linked by a special technical feature are answered as follows:

Applicants argument of the claims are linked by a special technical feature is not persuasive because Castagnoli et al. only teach ROP and does not teach redox center and applicants claims teach both ROP and redox center thus the claims show special technical

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feature. However evidence that the claims lack special technical feature is found in rejection heading under U.S.C.102 below. Applicants further argue that there would be no undue burden on the examiner to examine claims in groups I-IV directed to proteins comprising different **sequences having different SEQ ID NOs**. This is not persuasive because present practice of the PTO, since the search for each of these distinct groups having different **SEQ ID NOs** would be overlapping it would not be coextensive and need **enormous amount of searching time**, only one sequence having **ONE SEQ ID NO will be searched**. Therefore The restriction is maintained and made final. Therefore claims 1-5, 12-13, 14-15 , 21-25 and SEQ ID NO: 11 are for examination.

Priority

Acknowledgement is made of applicant's priority date based on PCT application application filing date of 12/03/2003 for PCT/GB03/05256 and foreign application filing date 12/04/2002 in United Kingdom, Application No. United Kingdom 0228301.8.

Objections

Claim 22 is objected to recite "an electrode" It should be "the electrode".

An appropriate correction is required.

Claim Rejections

35 U.S.C 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The claimed inventions 1-5 are rejected under 35 USC 101 because the claimed invention directed to non-statutory subject matter.

In the absence of the hand of man, naturally occurring genes are non-statutory subject matter (*Diamond v. Chakrabarty*, 206 USPQ 193 (1980)). The proteins in claims 1-5 may comprise natural substances like cytochrome -b or -c or cytochrome p450 types of enzymes. The rejection may be overcome by amending claims 1-5 to recite wording such as an isolated protein.

35 U.S.C 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 - indefinite in the recitation of "said ROP" because protein of claim 1 comprise α -helices of ROP; therefore it is not necessarily comprise an entire ROP protein.

Claims 15 - indefinite in the recitation of " $\Delta G_{\text{obs}}H_2O$ wherein $y > 3.0$ kcal/mol." makes the claim confusing because it is unclear what " $\Delta G_{\text{obs}}H_2O$ wherein $y > 3.0$ kcal/mol." Term means.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 12-13, 15, 21-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of protein molecules comprising any α -helices of ROP (repressor of primer) and redox center from any source. The specification teaches the structure of only a few single representative species of such proteins (SEQ ID NOs: 8, 11)s. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the Redox activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-5, 12-13, 15, 21-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein of SEQ ID NOs: 8 and 11 does not

reasonably provide enablement for any protein comprising 4 α -helices of ROP (repressor of primer) and any redox center. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-5, 12-13, 15 , 21-25 are so broad as to encompass any protein comprising 4 α -helices of ROP (repressor of primer) and any redox center. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of α -helices of ROP (repressor of primer) and any redox center broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of only a few proteins as claimed (SEQ ID N0s: 8 and 11).

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any protein comprising 4 α -helices of ROP (repressor of primer) and any redox center because the specification does not establish: (A) regions of the protein structure which may be modified without effecting ROP and redox activity; (B) the general tolerance of ROP and redox center to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any ROP and redox center residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any protein comprising 4 α -helices of ROP (repressor of primer) and any redox center. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of ROP activity, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988).

CLAIM Rejection - 35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 12-13, 15 , 21-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Gilardi et al. (Trend in Biotechnol. 2001, 19, 468-476). Gilardi et al. teaches 4 α -helices of ROP (repressor of primer) covalently bound to CyP450 (having metal (stable in two different oxidation state, i.e, iron, bound REDOX center) having redox mid-point potential of -485-+400mV wherein redox center is bound to ROP via his, glu, met or leu residues. Gilardi et al. also teach electrochemical sensor using said ROP-bound redox center coupled to an electrode (Pages 472-473). Gilardi et al. also teach electrochemical sensor using said ROP-bound non-metal type redox center such as FAD (page 475).

Applicants ROP comprising SEQ ID NO: 11 found to be novel.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Examiner, Art Unit 1652

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